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Block 13: Supplementary Note

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Iridium-Catalyzed Hydrosilylative Reduction of Glucose to Hexane(s)

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S Supporting Information

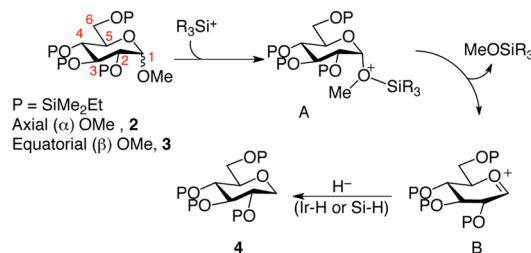
ABSTRACT: In light of diminishing petroleum feedstocks, there is significant interest in developing carbohydrate defunctionalization reactions. In this context we have examined the use of iridium pincer catalysts for the hydrosilylative reduction of sugars, and we report herein complete reduction of silyl-protected glucose to a mixture of hexane isomers.

The dwindling of petroleum resources has made carbohydrates attractive targets for renewable energy and chemical feedstocks.¹ Chemists have sought to defunctionalize sugars to simpler chemical feedstocks, which are compatible with modern chemical processes and infrastructure.² Despite significant effort, most systems relevant to carbohydrate defunctionalization utilize harsh conditions (high temperatures, pressures, and strong acids) and are generally low yielding for defunctionalized products.³ To date, the mildest systems for the reduction of carbon–oxygen bonds are hydrosilylative; however, for sugars these methods have been limited to defunctionalization at the activated C₁ position and take many hours.^{4–6}

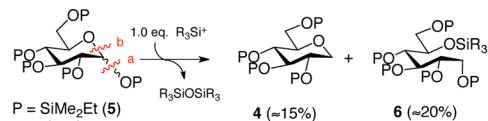
Brookhart has reported a cationic iridium pincer complex, **1**, which acts as a potent catalyst (<1 mol %) for the hydrosilylative reduction of alkyl ethers to alkanes (e.g., Scheme 1).⁷ In combination with triethylsilane, **1** mediates the complete reduction of primary and methyl ethers to the hydrocarbon. In the case of secondary ethers, only a single C–O cleavage occurs, and the secondary silyl ether is obtained. Despite these potential limitations, we surmised that the

enhanced stability of the C₁-carbocation of a sugar might support an alternative, Murai-like⁴ mechanism for the reduction of at least one secondary C–O bond in glucose (Scheme 2). In this scenario we anticipated C₁ reduction to be especially rapid.

Scheme 2

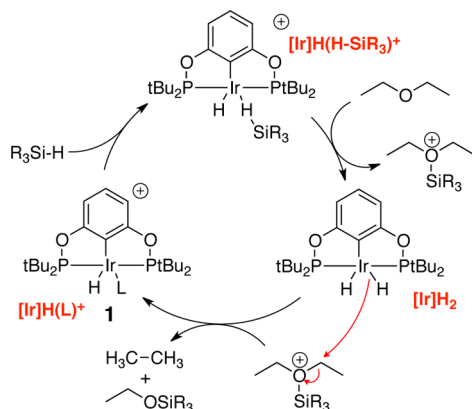


Initial experiments with 1% catalyst, 1.2 equiv of SiMe₂EtH, and the α - and β -anomers of silylated MeO-glucose (**2** and **3**), showed that reduction to **4** was rapid and complete within minutes (over 90% by NMR). Although both the α - and β -anomers reacted too fast to monitor rates, a competition between 1 equiv each of **2** and **3**, with 1 equiv of SiMe₂EtH (1% catalyst), established (by NMR) the near exclusive consumption of the equatorial (β) OMe isomer. The reduction of **5**, on the other hand, was substantially slower, requiring hours of reduction time and many equivalents of either SiMe₂EtH or the more reactive SiEt₂H₂⁸ for complete conversion. In addition to a slower rate, the selectivity for C₁ deoxygenation was compromised (see equation below).



Although reduction of **5** still yielded **4** through cleavage site “a”, a number of other products were also formed, including D-glucitol (**6**), which would require cleavage at site “b.” In situ monitoring by NMR spectroscopy of the reduction of **5** indicated that, like the C₁–OMe case, the β -anomer reacts faster (greater than 10 \times the rate), leading to the following comparative C–O hydrosilylation rates: C₁ equatorial, OMe > C₁ axial, OMe \gg C₁ equatorial, OSiR₃ > C₁ axial, OSiR₃ > C_n, OSiR₃ (n = 2,3,4,6). This trend can be rationalized by noting the importance of a basic ether in forming the key silyloxonium

Scheme 1



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isomers. MeO- sugars **2** and **3** proceed by selective C₁ reduction to **4**, whereas the persilyl glucose, **5**, is reduced to a mixture that includes **4** and the ring-opened sugar **6**. The hexane isomer distribution is sensitive to the C₁-substituent, with the 1-OMe-protected sugars **2** and **3** yielding mostly 2- and 3-methylpentane, whereas the C₁-OSiR₃, **5**, yielded mostly *n*-hexane. The reaction rate is affected by the silane, with the less hindered Et₂SiH₂ giving the fastest rates. Studies on the role of sugar, catalyst, and silane on the efficiency and hexane selectivity of this reaction are ongoing.

■ ASSOCIATED CONTENT

■ Supporting Information

Experimental procedures, carbohydrate protections/characterization, and NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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